LABORATORY REGISTRATION / SELECT AGENT TRANSFER PROGRAM

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OUTLINE

- What is the rule?
- What are Select Agents?
- Who needs to register?
- Registration process & requirements
  - Application
  - Inspections
- Do I need to register? - Exemptions

WHAT IS THE RULE?

Antiterrorism and Effective Death Penalty Act of 1996
Sec. 511. Enhanced Penalties and Control of Biologic Agents
Public Law 104-132; April 24, 1996

The Secretary of HHS shall, through regulation:

- Maintain a list of biological agents that have the potential to pose a severe threat to public health and safety.
- Establish procedures for the transfer of the listed biological agents, including measures to ensure:
  - Proper training and appropriate skills to handle agents.
  - Proper laboratory facilities to contain and dispose of agents.

Antiterrorism and Effective Death Penalty Act of 1996
(continued)

- Provide safeguards to prevent access to agents for criminal purpose.
- Establish procedures to protect public safety in the event of a transfer of an agent in violation of safety procedures.
- Provide availability of agents for legitimate purposes.

FINAL RULE

42 CFR Part 72.6
"Additional requirements for facilities transferring or receiving select agents"

Federal Register, Oct. 24, 1996
Effective date: April 15, 1997

TITLE 42 PART 72 - INTERSTATE SHIPMENT OF ETIOLOGIC AGENTS

Sec.
72.1 Definitions.
72.2 Transportation of diagnostic specimens, biological products, and other materials; minimum packaging requirements.
72.3 Transportation of materials containing certain etiologic agents; minimum packaging requirements.
72.4 Notice of delivery; failure to receive.
72.5 Requirements; variations.
72.6 Additional requirements for facilities transferring or receiving select agents.
72.7 Penalties.
Appendix A to Part 72 - Select Agents

PURPOSE OF THE REGULATION

Rule was designed to:

- Establish a system of safeguards to be followed when specific agents are transported;
- Collect and provide information on the location where certain potentially hazardous agents are transferred;
- Track the acquisition and transfer of these agents;
- Establish a process for alerting authorities if an un-authorized attempt is made to acquire these agents.

COMPONENTS OF THE REGULATION

Fundamental components:

1. A comprehensive list of select agents
2. Registration of facilities transferring these agents
3. Transfer requirements
4. Verification procedures including audit, quality control, and accountability mechanisms
5. Agent disposal requirements
6. Research and clinical exemptions

WHAT ARE SELECT AGENTS?

APPENDIX A TO PART 72 - SELECT AGENTS

13 Viruses
9 Bacteria
3 Rickettsiae
1 Fungi
12 Toxins

Genetically modified / genetic elements

APPENDIX A TO PART 72 - SELECT AGENTS

- **Viruses**
  - **Crimean-Congo haemorrhagic fever virus**
  - **Eastern Equine Encephalitis virus**
  - **Ebola viruses**
  - **Equine Morbillivirus (Hendra)**
  - **Lassa fever virus**
  - **Marburg virus**
  - **Rift Valley fever virus**
  - **South American Haemorrhagic fever viruses**
  - **Tick-borne encephalitis complex viruses**
  - **Variola major virus (Smallpox virus)**
  - **Venezuelan Equine Encephalitis virus**
  - **Viruses causing hantavirus pulmonary syndrome**
  - **Yellow fever virus**

APPENDIX A TO PART 72 - SELECT AGENTS

- Bacteria
  - *Bacillus anthracis*
  - *Brucella abortus, B. melitensis, B. suis*
  - *Burkholderia (Pseudomonas) mallei*
  - *Burkholderia (Pseudomonas) pseudomallei*
  - *Clostridium botulinum*
  - *Francisella tularensis*
  - *Yersinia pestis*

APPENDIX A TO PART 72 - SELECT AGENTS

- Rickettsiae
  - *Coxiella burnetii*
  - *Rickettsia prowazekii*
  - *Rickettsia rickettsii*
- Fungi
  - *Coccidioides immitis*

APPENDIX A TO PART 72 - SELECT AGENTS

- **Toxins**
  - **Abrin**
  - **Aflatoxins**
  - **Botulinum toxins**
  - **Clostridium perfringens epsilon toxin**
  - **Conotoxins**
  - **Diacetoxyscirpenol**
  - **Ricin**
  - **Saxitoxin**
  - **Shigatoxin**
  - **Staphylococcal enterotoxins**
  - **Tetrodotoxin**
  - **T- 2 toxin**

APPENDIX A TO PART 72 - SELECT AGENTS

- Recombinant Organisms/Molecules
  - Genetically modified microorganisms or genetic elements from organisms on Appendix A, shown to produce or encode for a factor associated with a disease.
  - Genetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins listed in this Appendix, or their toxic subunits.

WHO NEEDS TO REGISTER?

- Government Agencies
- Universities
- Research Institutions
- Commercial Entities
- Manufacturers & Suppliers

TITLE 42 CFR 72.6 APPLIES IF YOU:

Import into the U.S.
or
Transfer within the U.S.
an item on the Select Agent list

REGISTRATION PROCESS AND REQUIREMENTS

APPLICATION FOR REGISTRATION

- Designate Responsible Facility Official
  - Safety/Senior Management
- Provide information on facility and procedures
- Perform self-assessment based on requirements for handling select agents

REQUIREMENTS FOR HANDLING SELECT AGENTS

- For BSL 2-4 select agents:
  - Biosafety in Microbiological and Biomedical Laboratories, Third edition, May 1993.
- For toxin select agents:
  - 29 CFR 1910.1450 Occupational Exposure to Hazardous Chemicals in Laboratories.
- For recombinant select agents:
  - Guidelines for research involving recombinant DNA molecules (NIH Guidelines).

APPLICATION

Laboratory Registration and Select Agent Transfer Tracking System

FORMS TO BE COMPLETED

- Background Information/Certification & Signature
- Information on Select Agent (Section 1 & 2)
  - Viruses, Bacteria, Rickettsiae & Fungi
  - Recombinant DNA
  - Toxins
- Laboratory Assessment Instrument (Section 3)
  - CDC/NIH Biosafety in Microbiological and Biomedical Laboratories
  - NIH Guidelines for Research Involving Recombinant DNA Molecules
  - 29 CFR 1910.1450 – Occupational Exposure to Hazardous Chemicals in Laboratories

BACKGROUND INFORMATION/CERTIFICATION AND SIGNATURE

- Identify:
  - Facility
  - Responsible facility official (RFO)
  - Select agents
- Signature of RFO

INFORMATION ON SELECT AGENT Section 1

- Select appropriate form based on agent
- List select agent(s)
- Location
- Assessment
  - Diagnostic work/CLIA registration?
  - Small animal/Large Animal?
  - Large Scale?
  - Select requirements (BMBL, NIH Guidelines, or 29 CFR 1910.1450)

INFORMATION ON SELECT AGENT Section 2

- Individual responsible for laboratory
- Work that will be done
- Practices & Procedures:
  - Security
  - Training
  - Storage & Disposal
  - Spill & exposure management
- Facility Containment:
  - Sketch/floor plan
  - Air handling system
  - Biosafety cabinet/fume hood

LABORATORY ASSESSMENT INSTRUMENT Section 3

- CDC/NIH Biosafety in Microbiological and Biomedical Laboratories
  - BSL 2-4
  - ABSL 2-4
- NIH Guidelines for Research Involving Recombinant DNA Molecules
  - BSL 2-4
  - Large Animal BSL 1-4
  - Large Scale BSL 1-3
- 29 CFR 1910.1450 – Occupational Exposure to Hazardous Chemicals in Laboratories

REGISTRATION AND TRACKING

- Issued unique registration number
- Issued registration certificate
  - Valid for 3 years
- Issued EA-101 tracking form
  - Track shipments between facilities
- Inspection to verify registration / tracking information
  - Prior to registration, or
  - During the 3 year registration period

REGISTRATION MAY BE DENIED OR WITHDRAWN

- Facility not or is no longer capable of handling agents at appropriate BSL.
- Facility has handled covered agents in a manner in contravention of the BMBL.
- Facility has or intends to use agents in a manner harmful to human health.
- Facility does not comply with provisions of the regulation.

PENALTIES

42 CFR 72.7

- Individuals in violation of this part are subject to a fine of no more than $250,000 or one year in jail, or both.
- Violations by organizations are subject to a fine or no more than $500,000 per event.
- A false, fictitious, or fraudulent statement or representation on the Government forms required in the part for registration of facilities or for transfers of select agents is subject to a fine or imprisonment for not more than five years, or both for an individual; and a fine for an organization.

DISPOSAL

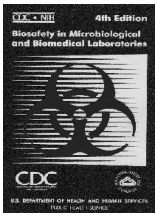
- Disposal of select agents must be at the facility, by known effective methods, and the facility should maintain records.
- CDC must be notified of the disposal or complete consumption of a select agent by completing EA-101.

SECURITY

- "Prudent laboratory practices suggest storing select agents such that unauthorized and unqualified persons cannot gain access to them and such that the responsible person can account for quantities stored. Prudent practice also suggests that storage be secure, including controlled access to the storage area and storage equipment."

BIOSAFETY IN MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES

4th Edition
JY Richmond & RW McKinney (eds.)
CDC/NIH, May 1999



http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm

BIOSAFETY IN MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES, Fourth edition, May 1999

- Incorporation into rule pending publication of new interstate shipping regulation by CDC
- Appendix F
  - Laboratory Security and Emergency Response for Microbiological and Biomedical Laboratories
- Appendix I
  - Guidelines for Work With Toxins of Biological Origin

DO I NEED TO REGISTER? EXEMPTIONS

- Attenuated vaccine strains
- CLIA certified laboratories
- Clinical specimens
- Toxins

EXEMPTIONS
ATTENUATED STRAINS

- "Attenuated strains of select agents approved for human vaccination purposes by FDA or other recognized national or international organizations will be exempt. All other attenuated, avirulent, or less pathogenic strains will not be exempt at this time."

VIRUS VACCINE EXEMPTED STRAINS
42 CFR 72.6, subpart (h)(1)(iii)

- Rift Valley fever virus
  - Vaccine strain MP-12
- Junin
  - Vaccine strain Candid #1
- Venezuelan Equine Encephalitis virus
  - Vaccine strain TC-83
- Yellow fever virus
  - Vaccine strain 17-D

BACTERIAL VACCINE EXEMPTED STRAINS
42 CFR 72.6, subpart (h)(1)(iii)

- FDA approved human vaccine strains
- USDA Title 9 CFR, Part 78.1
  - *Brucella abortus* 19; RB51.
- Other approved USDA vaccine strains

"CLIA" EXEMPTION
42 CFR 72.6, subpart (h)(2)

- "Clinical laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, (42 U.S.C. 263a) (CLIA), that utilize these select agents for diagnostic, reference, verification, or proficiency testing purposes are exempt from the provisions of Sec. 72.6."

"CLIA" EXEMPTION
for CLIA lab - non-CLIA lab transfers
42 CFR 72.6, subpart (h)(3)

- CLIA lab must be using the select agent for exempt purposes
- Non-CLIA lab must be registered
- Non-CLIA lab must complete EA-101

"CLINICAL SPECIMEN" EXEMPTION
42 CFR 72.6, subpart (h)(1) (i)

- "The agent is part of a clinical specimen intended for diagnostic, reference, or verification purposes. Isolates of covered agents from clinical specimens shall be disposed of in accordance with Sec. 72.6(i) after diagnostic, reference, or verification procedures have been completed;"

"CLINICAL SPECIMEN" EXEMPTION
42 CFR 72.6, subpart (h)(1) (i)
(continued)

- Intent was NOT to put the regulation between the physician and the patient
- Must be directly related to the health of the human or animal

"TOXIN" EXEMPTION

42 CFR 72.6, subpart (h)(1)(ii)

- For medical use
- National standard toxins required for biologic potency testing as described in USDA Title 9 CFR Part 113
- Preparations for biomedical research use at an LD_{50} for vertebrates of > 100 ng/kg body weight by IP in a mouse

REVIEW

SELECT AGENTS

- May pose a severe threat to public health and safety
- Existing regulations used for packaging, labeling, and shipping select agents
- U.S. facilities shipping and receiving must be registered with CDC
- CDC notified of all shipments (EA-101)

FOR MORE INFORMATION

- Laboratory Registration/Select Agent Transfer Program
  - Phone 404-639-4418
  - Fax 404-639-0880
  - E-mail lrsat@cdc.gov
  - Website
    http://www.cdc.gov/od/ohs/lrsat.htm

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